



Path-Dependent Evolution Versus Intentional Management of Investment Ties in Science-Based Entrepreneurial Firms

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This paper studies the role of entrepreneurs in investment tie formation in science-based entrepreneurial firms. Specifically, we address why investment tie formation is path dependent for some firms but more amenable to intentional management for others. Using longitudinal case studies, our evidence suggests that early investment tie formation is path dependent because scientific entrepreneurs typically approach only one or a few prospective investors from within their institutional context. Differences in experience between early investors affect the professionalization of entrepreneurial teams (or lack thereof), which influences the extent to which subsequent investment tie formation becomes more amenable to intentional management or remains path dependent.

Introduction

Science-based entrepreneurial firms play a key role in our modern, knowledge-based economies (Knockaert, Ucbasaran, Wright, & Clarysse, 2011). These firms not only compete on the basis of the ideas they generate, but also on their ability to attract resources that allow them to develop and commercialize their ideas (Janney & Folta, 2003). Investment ties with venture capital (VC) investors are one of the earliest and most critical ties formed by science-based firms because they provide both financial resources and value-adding services (Sapienza, Manigart, & Vermeir, 1996). Extant research on investment tie formation often takes the perspective of VC investors and portrays entrepreneurs as more or less passive bystanders (Katila, Rosenberger, & Eisenhardt, 2008). Rather than taking

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the perspective of VC investors, we take the *perspective of entrepreneurs* and ask the following questions: (1) How do scientific entrepreneurs influence early tie formation with VC investors; and (2) how do these early investment tie decisions influence subsequent tie formation?

These questions are important for at least two reasons. First, research that puts entrepreneurs in the foreground and shows how they influence investment tie formation is just developing (Hallen & Eisenhardt, 2012; Zhang, Souitaris, Soh, & Wong, 2008; Zott & Huy, 2007). Most of these studies highlight how entrepreneurs with relevant experience, business education, or prior working relationships may increase the pool of VC investors from which they can raise finance. Zhang et al. further show how industrial work experience increases the likelihood that entrepreneurs use their existing ties to search for start-up finance, while entrepreneurs without such experience search for VC finance through market mechanisms. Yet, the probability of raising VC finance through market mechanisms is low (Shane & Cable, 2002). Little is known on how entrepreneurs with limited business experience and few relevant ties successfully affiliate with VC investors. Nevertheless, many science-based firms are founded by scientists with little business experience or ties in the investment community (Ensley & Hmieleski, 2005) and for whom the value-adding services provided by VC investors are hence particularly valuable (Colombo & Grilli, 2010; Knockaert & Vanacker, 2013).

Second, few studies consider the impact of early VC investment partner decisions on future financial resource mobilization (Hsu, 2004). Opposing views exist with respect to the evolution of investment ties. One view suggests that entrepreneurs can manage the formation of ties as the resource requirements of their firms change, and this is irrespective of existing ties (Hite, 2005; Hite & Hesterly, 2001; Larson & Starr, 1993). Another view indicates that tie formation becomes increasingly path dependent and is heavily determined by the identity of early investors (Hallen, 2008). Recently, Zhang et al. (2008) showed heterogeneity in the extent to which *initial* investment tie formation is path dependent and relies on existing ties. In this study, we focus on the extent to which *future* tie formation becomes more path dependent versus more amenable to intentional management. By doing so, we contribute to a call for more longitudinal studies on how entrepreneurs influence tie formation (Slotte-Kock & Coviello, 2010; Zhang et al.).

We address our research questions by conducting nine longitudinal case studies to capture both the early search for investors and the subsequent evolution of investment ties. The lack of fine-grained insights on the role of entrepreneurs in investment tie formation (Slotte-Kock & Coviello, 2010) guided our decision to employ a case study approach. Our research context is that of biotech firms forming ties with VC investors. We first provide a brief theoretical background on tie formation, followed by a discussion of the case study method. Next, we develop the insights gained from the cases. Finally, we discuss our main findings from theoretical and practical perspectives.

Theoretical Background

At least two views exist to frame the formation of ties. One view argues that entrepreneurs have an ability to intentionally create, adapt, and control ties as their firms develop (Hite & Hesterly, 2001; Larson & Starr, 1993). Hite (2005), for instance, argues that entrepreneurs may proactively manage the evolutionary processes and paths of relationally embedded ties to enhance a firm's growth. Sophisticated entrepreneurs often take an active role in investment tie formation through the use of network-broadening actions and negotiation strategies (Hallen & Eisenhardt, 2012; Zott & Huy, 2007).

Overall, this view argues that entrepreneurs use strategies to increase partnering options and have the flexibility to choose among investors irrespective of prior relationships.

A second view argues that tie formation is path dependent due to factors outside the control of entrepreneurs (Gulati, Nohria, & Zaheer, 2000). The preferences of investors, for instance, may create and maintain path dependence in investment tie formation (Hallen, 2008). Specifically, VC investors prefer to form ties with firms located close to them, and headed by entrepreneurs with proven track records and prior working relationships (Beckman, Burton, & O'Reilly, 2007; Cumming & Dai, 2010; Hsu, 2007; Shane & Cable, 2002). From these early ties, future ties evolve as existing investors exhibit a tendency to restrict the formation of new ties to their direct partners and their partners' partners (Hallen; Meuleman, Lockett, Manigart, & Wright, 2010). This view implies that history has a great impact on the evolution of ties given that existing ties create a path-dependent environment.

This paradox of intentional management versus path-dependent evolution of ties has received limited attention (Hite & Hesterly, 2001). Some have argued that these two opposing views correspond to different phases in firm development, but even here scholars disagree. On the one hand, Hite and Hesterly argue that tie formation in new firms initially starts as highly path dependent, given the reliance of entrepreneurs upon their existing social network (Larson & Starr, 1993). However, as new firms move toward early growth and require different resources, the formation of ties becomes more amenable to intentional management. On the other hand, Hallen (2008) argues that intentional management might be effective during initial tie formation, whereas the formation of later ties is path dependent and primarily depends on a new firm's initial ties. Zhang et al. (2008), however, show that even within the start-up phase, heterogeneity exists with respect to the extent to which entrepreneurs rely on existing ties. The dominant view, which suggests that the stage of new firm development determines the path-dependent nature of tie formation, is hence incomplete.

Methods

As current theoretical perspectives offer limited guidance to understand heterogeneity in the path-dependent evolution versus intentional management of ties, formulating hypotheses for quantitative testing seem premature. We therefore opted for a case study approach, which is well suited to address how and why questions (Yin, 2003), and to engage in research that involves observations over time. Studying science-based firms as they develop helps us to explain how the successful and unsuccessful formation of investment ties unfolds over time (Van de Ven, 2007).

Research Design

To minimize external variation beyond the phenomenon of interest, it is suggested to choose one homogeneous research field (Eisenhardt, 1989a). Following this suggestion, we focused on investment tie formation in Flemish biotech start-ups. This has at least three additional advantages.

First, focusing on biotech start-ups allows us to focus on tie formation with VC investors. More traditional sources of finance, such as internal finance and debt finance, are often unavailable and even unsuitable for young biotech firms (Pisano, 2006). Before biotech firms can raise finance from pharmaceutical firms or public equity markets, they

first need to raise several rounds of VC (Pisano). In addition, given that biotech firms are characterized by high uncertainty, resource constraints are acute. In this context, forming investment ties is of heightened importance, and entrepreneurs are likely to devote significant time and energy to these activities.

Second, prior studies mainly attribute changes in the path-dependent nature of tie formation to firm development and performance (Hallen, 2008; Hite & Hesterly, 2001). In our context, it is unlikely that systematic differences in firm performance will drive heterogeneity in the path-dependent nature of investment tie formation. Even when biotech firms reach the stage where they conduct an initial public offering (IPO), these firms have typically not realized any sales yet and still need millions to develop uncertain technologies into products (Janney & Folta, 2003). Given that performance differences between biotech firms are difficult to evaluate at IPO, we expect this to be even more the case in our setting, which focuses on tie formation between founding and exit. As such, the biotech setting helps to identify processes other than firm performance that explain tie formation.

Third, Flemish biotech firms are typically founded by pure scientists. This is similar to other Continental European biotech industries but stands in contrast to the United Kingdom and the United States, where scientific entrepreneurs have often accumulated founding experience (Maurer & Ebers, 2006). Prior research has largely focused on investment tie formation in unique contexts, such as Silicon Valley or the Boston area, where entrepreneurs are often more experienced, or sampled cases where entrepreneurs received business education (e.g., Hallen, 2008; Hsu, 2004, 2007; Zott & Huy, 2007). Our study is set in a developing entrepreneurial ecosystem, where founding teams often lack business experience.

We followed the suggestion that research based on cases has between 4 and 10 cases to reach theoretical saturation (Eisenhardt, 1989a). We selected nine cases from start-ups in the biotech industry controlling for location, firm origin, and market sentiment. Biotech start-ups are defined as dedicated biotech firms, active in research and development, and founded between 1999 and 2003 in Flanders. This implies that firms were at maximum 5 years old at the time of initial data collection. Table 1 provides information on the cases (the names of the firms are disguised to ensure confidentiality).

Data Collection

The first phase of data collection consisted of semi-structured interviews conducted in 2003 with founding entrepreneurs and senior managers in biotech firms. Interviews took between 90 and 120 minutes, and followed a pretested interview guide. During the interviews, we asked for background information, such as composition of the entrepreneurial team, alliances, and products in the pipeline. We then asked informants to provide information with respect to the financing of their firms. We also conducted interviews with investors that offered finance to the cases studied. We discussed the different phases in the investment process from deal origination through exit. A second wave of interviews in 2004 specifically focused on the formation of investment ties over time. We asked entrepreneurs to discuss chronologically the financing history of their firms. Access to yearly financial accounts allowed interviewers to prepare a financing timeline in advance of each interview, capturing the history of the investment ties formed. During the interviews, we also discussed the finance unsuccessfully applied for and the finance sources that entrepreneurs were not willing to consider. In total, we conducted over 40 interviews, including pilot interviews, 15 interviews with biotech entrepreneurs and managers, 10

Table 1

Description of Cases Studied

Case name	Founding year	Firm origin	Market sentiment [†]	Activity profile	First round finance (in KEuro)	Pre-exit finance (in KEuro)	Exit (year)	Employment (in FTE) in founding year	Employment (in FTE) in 2006	Number of patents in EPO database (until 2006) [‡]
Aptanomics	2002	Research institute	Cold	Platform technologies, diagnostics, and therapeutics	62	70,000	IPO (2007)	6	59	22
Genom	1999	Corporate	Cold	Platform technologies and therapeutics	4,450	29,400	IPO (2005)	16	67	10
Theraphosis	2000	Academic	Hot	Therapeutics	600	28,800	IPO (2007)	3	33	17
AC Pharma	2002	Academic	Cold	Platform technologies and therapeutics	4,500	6,750	Trade sale (2006)	2	10 [‡]	19
Pharmaleads	2000	Academic	Hot	Therapeutics and platform technologies	1,100	2,600	No	5	3	0
Myosic	2003	Academic/Corporate	Cold	Diagnostics	1,500	1,500	Bankrupt (2006)	1	3 [‡]	0
Entomed	2002	Academic	Cold	Platform technologies	470	1,200	No	1	4	2
Irogene	2002	Corporate	Cold	Therapeutics	350	350	No	4	N.A. [§]	0
I-Zyme	2002	Research institute	Cold	Platform technologies, and industrial and environmental biotech	62	62	No	2	N.A. [§]	0

Notes: [†] Market sentiment is defined as “hot” when initial venture capital (VC) was raised between 1999 and 2000, which were record years in terms of amount of finance invested by VC investors (European Venture Capital Association [EVCA], 2005). It is defined as “cold” when initial VC was raised between 2002 and 2003, a period during which VC investments decreased dramatically, especially in high-tech industries. [‡] Data from 2005. More recent data were not available due to failure or acquisition. [§] N.A. indicates data are not available. However, as wages and remunerations paid by Irogene and I-Zyme remained stable or even decreased, employment is unlikely to have increased. ^{||} At start-up, cases had no patents on their name yet, but all had an exclusive license on a patent or patent portfolio from the university or parent company.

Source: Financial accounts, interviews, European Patent Office (EPO), and company websites. FTE, full-time equivalent; IPO, initial public offering.

interviews with investors, and additional telephone interviews with biotech team members to cross-check information obtained from the interviews.

We limit recall bias by studying firms that were at maximum 5 years old at the time of initial data collection and where the formation of investment ties are major events (Zhang et al., 2008). Triangulation of multiple data sources further helped to minimize the effects of retrospection (Yin, 2003). In addition to interviews, we had access to (1) the business plans that some of the firms used to raise early finance, (2) financial statement data and statutory required publications on capital increases and shareholder structure, and (3) archival data, including websites and business publications.

Data Analysis

Transcriptions alone totaled over 700 pages. We started by building individual cases, synthesizing the interview transcripts and archival sources. Case histories were used for within-case and cross-case analyses. The within-case analysis focused on the successful and unsuccessful formation of investment ties, and provided important facts for the individual cases. Within-case analysis allowed us to describe tie formation as experienced by a single case. Next, the conclusions from each individual case were considered information needing replication by other cases (Yin, 2003). We used cross-case analysis techniques to look for similarities and differences across cases.

Results

Entrepreneurship research by its very nature involves the study of “beginnings” (Forbes, Borchert, Zellmer-Bruhn, & Sapienza, 2006), and hence we start the presentation of our results with detailing the mechanisms that drive the search by scientific entrepreneurs for their early VC investors. Next, we proceed with how these early decisions influence subsequent tie formation.

The Search for Early Investors by Scientific Entrepreneurs

Research has typically portrayed VC investors as the more powerful actors in tie formation (Katila et al., 2008). It is often assumed that once entrepreneurs decide to raise outside finance, VC investors can select from the entire pool of firms that are willing to raise outside finance (Eckhardt, Shane, & Delmar, 2006). VC investors, for instance, are described to exhibit a local bias: They mostly invest in geographically close firms (Cumming & Dai, 2010). Within their local markets, VC investors typically select entrepreneurs with proven reputations and prior working relationships (Beckman et al., 2007; Hallen, 2008; Hsu, 2007; Shane & Cable, 2002). In this stream of research, entrepreneurs are portrayed as passive and largely unable to influence the identity of their early VC investors.

Recent studies have focused on the role of entrepreneurs in the formation of investment ties, but have largely focused on entrepreneurs with relevant experience, business education, or existing ties in the finance community (Hallen & Eisenhardt, 2012; Zott & Huy, 2007). These studies show how more sophisticated entrepreneurs take deliberate actions to *broaden* the pool of prospective investors. In our setting, most entrepreneurs are scientists without business experience or education. Interestingly, our data revealed that the search behavior of entrepreneurs in science-based firms *constrains* the pool of VC

Table 2

The Impact of Scientific Entrepreneurs on Early Investors

	Facts	Illustrative quotes	IL [†]	PR [†]
Aptanomics	Aptanomics raised finance from a highly experienced investor. This experienced investor has financed nearly all spin-offs from the research institute.		✓	
Genom	Corporate spin-off getting finance from parent company. Did not look for other potential equity investors.	"The CEO did not need to look for money, it was provided by the two parent companies."	✓	
Theraptosis	University spin-off getting finance from university fund. Did not look for other potential equity investors.	"It was the logical choice in the case of a spin-off."	✓	
AC Pharma	University spin-off getting finance from university fund and its shareholders.	"The firm is a university spin-off and one of our investors is the university spin-off fund. . . . All initial investors in our firm are also shareholders of the university fund."	✓	
Pharmaleads	University spin-off getting finance from university funds. Did not look for other potential equity investors.	"It is the norm for spin-offs from universities to start talking to the seed funds of universities. With the university fund we had the most obvious link."	✓	
Myosic	Spin-off getting finance from a corporate and university fund. Did not look for other equity investors.	"When searching for funding it appeared to be logical to have resources from the investors with whom the company and entrepreneur already had contacts."	✓	✓
Entomed	CEO contacted a business professor and relied solely on him to locate an investor. There was a friendship between the university professor and the senior investment manager of the initial investor.			✓
Irogene	Corporate spin-off getting finance from parent company. Tried to attract finance (unsuccessfully) from a small number of investors, besides the parent company.	"Contacts were first initiated with a university seed fund. When they were not willing to invest the parent company provided finance."	✓	
I-Zyme	Spin-off getting start-up finance from research institute. Did not look for other equity investors, besides some loose contacts.	"The institute had the idea to spin-off the company and was willing to invest. Afterwards, there were some contacts with business angels, but not more, things did not get any further."	✓	

Notes: [†] Where IL indicates institutional linkage(s) and PR indicates personal relationship(s).

Source: Interviews.

CEO, chief executive officer.

investors that could invest at an early stage. Specifically, Table 2 shows that entrepreneurs limited the number of investors they approached during their search for early finance. These investors were either related to the firm through institutional linkages or to a lesser extent related to the entrepreneurs through existing personal (direct or indirect) ties. Our cases thereby suggest that early investment tie formation in science-based firms is highly path dependent, given the reliance of entrepreneurs upon existing ties.

A possible cause of this restricted search behavior is that entrepreneurs had no alternative as a consequence of constraints imposed by the supply side of the market (e.g., the investment preference of VC investors). While partially possible, this explanation is doubtful. Scientific entrepreneurs often refrained from testing the market for credible alternatives. For example, the chief executive officer (CEO) of Pharmaleads, a university

spin-off, did not contact other investors. He stated, “We did not need to contact other VC investors or business angels because we were able to raise equity from the university fund.”

Why do scientific entrepreneurs then limit their search for early investors to one or a few investors? First, science-based firms are typically embedded in universities, research institutes, or parent companies, bringing about their own culture, norms, and procedures (Moray & Clarysse, 2005). Our cases suggest that informal norms direct entrepreneurs’ early search efforts toward VC investors located within their founding context. When entrepreneurs justify actions with the claim that “everybody does it this way,” they refer to institutionalized activities (Oliver, 1997). In Pharmaleads and Theraptosis, two university spin-offs, the CEOs justified why they only searched for finance from university funds by indicating that it is the norm for spin-offs to do so. The CEO of Pharmaleads stated: “It is the norm for university spin-offs to start talking to the seed fund of universities.”

Second, the search for investors in imperfect markets is a function of the amount of information that is available to entrepreneurs, and information deficiencies limit entrepreneurs’ set of choices (Seghers, Vanacker, & Manigart, 2012). Information asymmetry and bounded rationality entail that scientific entrepreneurs are unlikely to be aware of all potential investors and are unable to negotiate with all these investors (Eisenhardt & Zbaracki, 1992). Moreover, cognitive limits make it unlikely that entrepreneurs will enter negotiations with all potential investors. Boundedly rational entrepreneurs, therefore, tend to rely on rules and norms when approaching early investors. A major benefit of relying on institutional linkages is that they help entrepreneurs in identifying where the needed resources are available (Hite & Hesterly, 2001; Rangan, 2000). The CEO of AC Pharma indicated: “There are two reasons why the firm found its initial investors relatively easily. One reason is that the firm is a university spin-off and one of our investors is the university spin-off fund . . . and all initial investors in our firm are also shareholder of the university fund.” Thus, scientific entrepreneurs often find it easier to locate prospective investors within their institutional context.

In addition, entrepreneurs possess private information, which makes funding by VC investors challenging (Eisenhardt, 1989b). The risk of expropriation makes scientific entrepreneurs especially reluctant to disclose critical information when searching for early investors. The following quotes of investors illustrate that the transfer of information is perceived as a problem by scientific entrepreneurs: “Particularly pre-investment, entrepreneurs are wary to disclose all information to us. . . . We live in a competitive world and have a large number of portfolio firms. It happens that a firm that looks for finance is a competitor of one of our portfolio firms or that there is at least a partial overlap. Therefore, information transfer is often a problem . . .” Disclosure is less problematic if funding is sought from VC investors within the firm’s founding context, as goal alignment makes entrepreneurs perceive lower agency risks *vis-à-vis* these investors. The following quote from an investor illustrates: “Unwillingness to provide information is something which is more common with external entrepreneurs. It is less of a problem if we work with scientists from our own university.” Information problems and perceived agency risks further contribute to limiting entrepreneurs’ early search for funding to their institutional context.

Overall, early investment tie formation by scientific entrepreneurs is highly path dependent, given the reliance of these entrepreneurs upon preexisting linkages. Thus:

Proposition 1: Scientific entrepreneurs are likely to limit their search for prospective VC investors to those investors located within their institutional context because of institutional norms, bounded rationality, and informational asymmetries.

Following proposition 1, investment tie formation in science-based firms can be viewed as a multistage selection process, in which scientific entrepreneurs select the pool of VC investors they want to approach, and VC investors subsequently select from the pool of firms that are presented to them. This behavior limits the pool of early-stage firms VC investors have access to. The search process defined here is a further refinement of the selection model presented by Eckhardt et al. (2006), who assume that investors have access to all firms once they are willing to raise outside finance.

Early Investor Decisions and the Ability of Entrepreneurs to Influence Investment Tie Formation

A key question is whether the early choice of investors has implications for subsequent investment tie formation (Cumming & Dai, 2013; Hsu, 2004; Zhang et al., 2008). Our cases show how entrepreneurs typically become more comprehensive in their search for investors as firms develop. For instance, we observed that it is not uncommon for entrepreneurs to contact 20 investors when preparing for follow-on finance rounds. Nevertheless, although entrepreneurs become more comprehensive in their search, we also observe that the identity of early investors has a great impact on the extent to which future investment tie formation becomes more amenable to intentional management or remains path dependent. Later, we elaborate on this finding.

Differences in Tie Formation Between Science-Based Firms Backed by Experienced Versus Inexperienced VC Investors. Our cases suggest that the experience of early investors influences the degree to which entrepreneurs can intentionally manage subsequent tie formation. Table 3 shows investor characteristics and the finance rounds in which they participated. It highlights how subsequent investment tie formation is very different between firms affiliating early on with experienced VC investors and firms without such experienced investors. We define VC investors as experienced when they (1) actively target and invest in biotechnology firms, and (2) have a team dedicated to evaluate and follow up biotech proposals.

Three observations emerge from Table 3. First, science-based firms backed by experienced investors during their first or second finance round raise larger amounts of follow-on finance on more occasions compared with firms backed by inexperienced investors. Second, science-based firms backed by experienced investors in an early round are able to attract a larger number of VC investors compared with firms backed by inexperienced investors. Third, science-based firms backed by experienced investors typically raise follow-on finance from other experienced investors. When inexperienced investors join an experienced investment syndicate, they do not take up a lead position (Lerner, 1994). In addition, when local experienced investors contribute finance, international-experienced VC investors are more likely to join in later rounds. In contrast, science-based firms backed by inexperienced investors often raise follow-on finance from other inexperienced investors. The founder of Entomed indicated that it became clear after the first round of finance from an inexperienced investor that for subsequent rounds, “experienced investors would be better because of their expertise and help for management.” Despite his attempts to attract more experienced investors, he failed to do so. In sum, cases initially backed by more experienced investors have access to a broader pool of high-quality investors compared with cases backed by inexperienced investors.

The following quotes further illustrate how science-based firms starting with experienced investors have more partnering options compared with firms starting with

Table 3

Investment Tie Formation Over Time by Type of Investor

Case name	Type of investor and financing round in which they participated						Pre-exit finance (in KEuro)
	Domestic-experienced VCFs	International-experienced VCFs	Academic VCFs	Bank VCFs	Other inexperienced VCFs	Parent company/institute	
Aptanomics	1,2,3,4	2,3,4	—	4	—	—	70,000
Genom	—	2	—	—	—	1	29,400
Theraptosis	2,3	2,3	1,2,3	2,3	3	—	28,800
AC Pharma	1,2	—	1,2	1,2	—	—	6,750
Pharmaleads	—	—	1,2	2	—	—	2,600
Myosic	—	—	1	—	—	1	1,500
Entomed	—	—	2	—	1,2,3	—	1,200
Irogene	—	—	—	—	—	1	350
I-Zyme	—	—	—	—	—	1	62

Notes: The numbers in bold indicate finance rounds that occurred before the main data collection (the interviews). The numbers in italics indicate finance rounds that occurred afterward. If cases raised new finance, we should notice this in the statutory required publications and financial statements, which firms are obliged to file by law. The upper half of the table includes firms that raised finance from experienced VC investors; the lower half of the table include firms that raised finance from inexperienced venture capital (VC) investors. We labeled VC firms (VCFs) as experienced VCFs when they (1) actively target investments in biotechnology firms, and (2) have a team dedicated to evaluate and follow up biotech proposals. Inexperienced VC investors comprise VCFs investing only sporadically in biotech without a team dedicated to biotech. In our context, these include some independent generalist VCFs, university funds, and VC subsidiaries of banks. In the case of corporate spin-offs, the parent company is typically involved in providing start-up finance.

inexperienced investors. The CEO of Aptanomics, backed by experienced investors from start-up, contacted about 50 VC investors to raise follow-on finance as the investment climate was bad. He thought “better contact more than less,” expecting that 10% would respond positively. “This would have given us 5 investors to negotiate with, which was fine. Surprisingly, 90% responded positively. We ended up with more than 40 investors to talk with and that was a problem. So, choices had to be made.” The CEO of Theraptosis, backed by an experienced investor, commented on his search for a subsequent finance round: “We talked with some 20 VC investors” and “The firm eventually raised 3 million euro more than it initially expected to raise.” On the other hand, the CEO of Pharmaleads, backed by inexperienced investors, mentioned: “Pharmaleads was developing its drug discovery strategy. However, this could only be achieved if additional financial resources were raised. European VC investors were contacted, among which [were] UK VC investors, because there are many knowledgeable VC investors in the UK.” Pharmaleads was unable to raise finance from new investors, however. “As a consequence of not getting funding, Pharmaleads was forced to restructure itself and scale down.”

In sum, the above suggests that science-based firms backed by experienced investors face few constraints induced by past partnering decisions when attempting to form new investment ties. These findings coincide with Hite and Hesterly (2001) who portray tie formation as amenable to intentional management. In the cases where firms raise early finance from inexperienced investors, investment tie formation becomes more path dependent, however. These findings correspond with Hallen (2008) who indicates that investment tie formation becomes increasingly path dependent.

The Differential Role of Experienced and Inexperienced Investors in Professionalizing the Management Team of Portfolio Firms. Why is investment tie formation more amenable to intentional management in firms initially backed by more experienced investors but more path dependent in firms initially backed by inexperienced investors? Prior research, which focused on the perspective of VC investors, argues that potential investors are more likely to collaborate with other investors that they know from prior investments (Hallen, 2008; Meuleman et al., 2010). Ferrary (2010) further argues that exchanges between VC investors are based on a reciprocity that follows the principles of gift exchange theory. Experienced investors, by virtue of being actively involved in the industry, have more ties to other investors within the biotech investment community (Gompers, Kovner, Lerner, & Scharfstein, 2008) and have more legitimacy, allowing them to enter more syndicate relationships (Hopp, 2010). The stronger network position of experienced investors therefore benefits their portfolio firms when searching for follow-on finance. Firms connecting with inexperienced investors, however, will be more constrained in their options for follow-on finance due to the limited social capital of their initial investors.

Our cases suggest that the (lack of) social capital of early investors only partially explains our observations. Differences in firm professionalization driven by different VC investors also impact subsequent investment tie formation. Although prior research indicates that VC investors as a group play an important role in firm professionalization by appointing outsiders as CEO (Beckman & Burton, 2008; Hellmann & Puri, 2002), our cases illustrate that especially experienced VC investors play a vital role in professionalizing firms by shaping their management team, while inexperienced investors play a more limited role. This is in line with recent research that highlights heterogeneity in value-adding activities among VC investors (Bottazzi, Da Rin, & Hellmann, 2008; Knockaert & Vanacker, 2013).

Table 4

Key Changes in the Management Team Relating to the Chief Executive Officer (CEO) and Chief Financial Officer (CFO) Functions

	Professional CEO		Professional CFO	
	Timing	Description	Timing	Description
Aptanomics	Start-up year	CEO hired, with extensive experience in both European and U.S. biotechnology start-ups under impetus initial investor.		
	4 years after start-up	New CEO hired with a successful track record in creating company value and attracting finance both in private and public area.	4 years after start-up	Professional CFO hired.
Genom	Start-up year	CEO hired from parent company.	5 years after start-up	Professional CFO hired.
Theraptosis	Start-up year	CEO with consulting background in the biotech industry next to scientific entrepreneur.	7 years after start-up	New professional CFO hired.
AC Pharma	Start-up year	CEO hired under impetus initial investor with consulting background in the biotech industry.		None.
	2 years after start-up	New CEO hired with consulting background in biotech industry. Previously, informal advisor to venture capital funds.		
Pharmaleads		None.		None.
Myosic	2 years after start-up	New CEO hired under impetus initial investor. Previously cofounded an ICT company and a medical software venture.		None.
Entomed		None.		None.
Irogene		None.		None.
I-Zyme		None.		None.

Notes: The upper half of the table includes cases that raised finance from experienced venture capital (VC) investors; the lower half of the table includes cases that did not raise finance from such investors.

Source: Interviews and press releases.

ICT, information and communications technology.

Table 4 summarizes key changes in management. This table shows that in firms backed by experienced investors, a CEO is typically hired shortly after the initial investment. In Aptanomics, the experienced VC investor played a crucial role in hiring a professional CEO with considerable experience in biotech shortly after founding. This manager previously held key positions in both domestic and foreign biotech firms. Similar changes to the scientific founding team were observed in AC Pharma. In Genom, an experienced manager was transferred from one of the successful biotechnology parents. Experienced VC investors are not only active around the time of their initial investment, but they also initiate changes in the team when the firm gets closer to an exit, for instance, through hiring a professional chief financial officer.

Table 4 suggests that professionalization seldom occurs in firms backed by inexperienced investors. In Pharmaleads and Entomed, both firms backed by inexperienced VC investors, no changes took place in the management team. The same holds for Irogene, which was financed by its parent and for I-Zyme, the first spin-off from a research institute and initially financed by this institute. In Myosic, the inexperienced academic investor and the corporate investor had doubts about the management qualities of the scientific founder.

Despite these concerns, investors accepted that the founder took the lead over the firm. It was only once his shortcomings became visible through weak progress some 2 years after founding that a professional CEO was hired. This new CEO, however, had little specific experience in managing young dedicated biotech firms.

Professionalization of the Management Team and Investment Tie Formation in Science-Based Firms. The level of professionalization initiated by investors influences the formation of new investment ties. In firms backed by inexperienced investors, scientific founders often remain in their firms and continue to play a central role in negotiations with potential investors. This leads to a situation of stunted learning, which culminates in a number of disadvantages and thereby limits the flexibility to form ties with new investors. More specifically, many scientific founders fail to fully develop the competencies required to manage a business, including the ability to negotiate and raise large amounts of follow-on finance (e.g., Vohora, Wright, & Lockett, 2004). For example, in our interviews with scientific entrepreneurs, we sometimes had to clarify the meaning of common terms used by professional investors. Some scientific founders asked: “Could you please explain the term cash burn rate?” or “What is the difference between common and preferred stock?” Further, investors often complain that the business plans of biotech firms headed by scientists are not accessible because they are too focused on the technology. The following quotes illustrate: “One of the most important shortcomings of biotech business plans is an underdeveloped business model. While there is often a very interesting scientific concept, people have not thought adequately about how the technology can be translated into an economic model. Inexperience makes that timelines and financial plans are unrealistic . . .” and “I can give examples of business plans from firms that exist for over five years . . . when one looks at those business plans . . . it still looks like these are written by scientists that work on a scientific project.”

These quotes illustrate that scientific founders often lack the social competence or ability to effectively interact with investors (Baron & Markman, 2003), and hence the possibility to establish investment ties with new partners is limited (Brinckmann, Salomo, & Gemuenden, 2011). As a result, firms affiliating early on with inexperienced investors typically find it difficult to obtain follow-on finance from new investors. Investment tie formation becomes increasingly path dependent and may even lead to a lock-in situation, where entrepreneurs find no other funds but from their existing investors.

Not all firms experience these problems. Firms backed by experienced investors are more likely to enter into a cycle of accumulating advantages. Experienced investors are more likely to strengthen the founding team with experienced managers and finance specialists, which benefits firms in their search for finance from new investors. Maurer and Ebers (2006) indicate that firms require specialization within the entrepreneurial team in order to facilitate changes in their social capital and achieve high growth. Our cases illustrate how professional managers’ social competence cannot be matched by that of scientific entrepreneurs. Higher levels of social competence assist professional managers in gaining the trust and confidence of persons with whom they interact and, therefore, help them in their efforts to raise capital (Baron & Markman, 2003). Throughout our interviews with professional managers, we observed how they possessed relevant knowledge on the VC industry, its trends, and its structure. This enabled them to effectively interact with potential investors, for example, by adapting themselves to a new context. This social adaptability is one aspect of their social competence (Baron & Markman). The CEO of Genom, for instance, recognized that the main business of his firm was out of vogue when

he approached VC investors. He decided to write a business plan making the firm (at least look) more attractive to investors given the current investment trends. The firm eventually received successful offers from multiple investors.

Professional biotech managers have a track record of experiences with raising VC and as such developed a tested toolbox with routines to approach new investors (Bingham, Eisenhardt, & Furr, 2007). These professional managers are clearly more effective in interacting with VC investors. Hence, their social competence or ability to interact with unknown investors is higher compared with that of scientific entrepreneurs (Zhang et al., 2008). This helps to explain why investment tie formation becomes more amenable to intentional management in firms backed by more experienced investors. Therefore:

Proposition 2: Experienced investors are more likely to professionalize the entrepreneurial team in science-based firms compared with their inexperienced counterparts, which enhances the social competence of the entrepreneurial team, which in turn makes investment tie formation more amenable to intentional management (or less path dependent).

The earlier findings strengthen insights from prior research focusing on the partnering preferences of VC investors. Firms backed by experienced investors have more partnering options. This is not simply due to the social capital of their experienced VC partners (which is mainly the focus of prior research), but also because the firms themselves have more competencies to negotiate with potential investors thanks to a stronger professionalization of the entrepreneurial team. Firms backed by inexperienced investors, however, have fewer partnering options. This is not only because of the limited network of their early investors but also because of their inability to negotiate with new investors, as inexperienced investors are less likely to initiate changes to the entrepreneurial team. Thus:

Proposition 3: The partnering preferences of VC investors and VC investors' professionalization activities in science-based firms have a mutually reinforcing impact on the subsequent formation of investment ties and its amenability to intentional management.

Alternative Explanations. Is it the experience of early VC investors that drives subsequent tie formation, or do differences in firm quality drive our findings? Differences in firm quality may matter to some extent but are unlikely to fully drive our findings. First, all our cases had high growth ambitions at start-up. Entomed, for example, planned to develop into a professional biotech firm in 2–3 years after founding, employing 25–30 people. In Myosic, the founder envisioned raising some 10 million euro in follow-on finance. Despite their high growth ambitions at start-up, scientific founders backed by inexperienced investors were unable to realize them. Second, we measured early quality signals, including human capital, alliance capital, technology, and target market (Baum & Silverman, 2004). We found no systematic differences in these early quality signals for firms that end up with experienced versus inexperienced investors (a detailed comparison table is available from the authors upon request). Finally, our research context also minimizes the concern that differences in the performance of firms backed by experienced versus inexperienced investors explain the extent to which future investment tie formation becomes more or less amenable to intentional management. Although we observe that some cases exhibit high growth and other low growth, it is not possible to equate growth with performance (Davidsson, Steffens, & Fitzsimmons, 2009). Biotech firms may exhibit low performance despite showing high growth rates. Moreover, finance is more likely to drive growth in the biotech context rather than the other way around.

We do not argue that investment tie formation is entirely deterministic. In line with studies showing entrepreneurial agency in tie formation, it may still be possible for a science-based firm to raise VC from an experienced VC later on despite having inexperienced investors at start-up (e.g., Cumming & Dai, 2013). Theraptosis is a good illustration. This firm raised start-up finance from an inexperienced university fund but subsequently raised finance from highly experienced investors. Three enablers are worth noting in this case. First, a more experienced manager was working together with the scientific founder from start-up. Second, with the finance raised at start-up, the firm reached all important milestones, hence demonstrating its managerial and technological abilities. Third, the CEO used an insightful strategy to approach experienced investors. While he was in a weak position to approach experienced investors directly, he resorted to network leverage strategies (Gargiulo, 1993). He approached not only the shareholders of the university-related investor (mostly bank-related investors), but also more experienced investors that previously worked together with the shareholders of the university fund. Theraptosis is the only case, however, which started with an inexperienced investor and subsequently raised finance from experienced investors.

Discussion and Conclusions

We studied how scientific entrepreneurs influence early tie formation with VC investors and how these early ties influence subsequent tie formation. By doing so, we add to the VC literature in several ways. First, prior studies have either taken the perspective of VC investors when studying investment tie formation (Katila et al., 2008) or focused on how sophisticated entrepreneurs may increase the pool of VC investors that are willing to provide finance (Hallen & Eisenhardt, 2012). We show that in science-based firms, where entrepreneurs generally have limited business experience, entrepreneurs often restrict their search for early VC investors to one or a few investors located in their founding context. Our findings add nuance to the two-stage selection model of Eckhardt et al. (2006) who assume that investors have access to all firms once they are willing to raise outside finance.

Second, VC syndication studies often assume that once firms attract finance from experienced investors with broad networks, new investors join through a semiautomatic process, where new investors will provide finance based on the identity of early investors (e.g., Hallen, 2008; Meuleman et al., 2010). We show that this is only part of the story. Inexperienced investors are more likely to keep scientists in the position of managing their firms, which leads to a situation of stunted learning, where scientific founders lack the capabilities to negotiate with investors. Firms backed by inexperienced investors indeed raise limited, if any, follow-on finance typically from a limited pool of inexperienced domestic investors and have limited options to choose between investors. Experienced investors are more likely to professionalize entrepreneurial teams, which contributes to the competence of these teams to negotiate with investors. This leads to a cycle of accumulating advantages, where firms backed by experienced VC investors can benefit from the latter's social capital, and professional managers use their social competence to capitalize on this. Firms backed by experienced investors indeed raise more finance on more occasions from a broader set of investors and have more options to choose between investors. We also add to the literature on path dependence versus intentional management of ties by showing how investment tie formation becomes more

or less amenable to intentional management depending upon the experience of early investors.

This research has a number of limitations that lead to directions for future research. First, we showed that one key difference between experienced and inexperienced investors is that the former are more likely to introduce changes to the entrepreneurial team. This influences the capabilities of teams to negotiate with investors, which further explains why subsequent investment tie formation is more or less amenable to intentional management. The entire spectrum of issues associated with tie formation (and differences between firms backed by experienced or inexperienced investors) is too extensive to be explored in one article. Following the suggestion of Van de Ven (2007), we put some issues in the foreground, but other issues in the background. We are mindful of the wider range of issues, however, such as the differential role of experienced and inexperienced investors in the board of directors (Rosenstein, Bruno, Bygrave, & Taylor, 1993). Another aspect that warrants more research relates to the contracts used by different investors. Strong contracts allow for good governance by VC investors (Cumming & Johan, 2009), which may also influence future investment tie formation. Future studies may focus in greater detail on what different VC investors are doing differently within their portfolio firms and how this influences firm-level processes such as investment tie formation.

Second, because our research setting is a special case, our conclusions must be tentative. It is not clear how our conclusions might relate to firms in other industries. As our focus was on theory building, further research is needed to formulate the propositions we developed into hypotheses and to test them on large samples (Yin, 2003). However, the framework we developed suggests a rich avenue for further research on how entrepreneurs with limited business experience, together with their early investors, affect the formation of investment ties. Specifically, future work may focus in more detail on the conditions under which entrepreneurs limit their search for finance to one or a few investors and when they engage in a broader search. Future work also needs to focus more on how the interaction between VC investor characteristics and portfolio firm characteristics influence subsequent investment tie formation. A good example in this direction is the study by Cumming and Dai (2013), which shows among other things that firms with upwardly revised perceived quality are more likely to switch to more reputable lead VC investors relative to existing lead VC investors. Further, future studies could look into how entrepreneurs manage lock-in situations with existing investors. Lastly, a question that deserves more attention is how some young and inexperienced VC investors manage to occupy privileged positions in the overall network of the VC industry and attract high-quality deal flow.

This study contributes to practice by improving entrepreneurs' understanding of investment tie formation in science-based firms. Our results point entrepreneurs to the relevance of searching for finance from investors outside their institutional context, especially when investors in the institutional context are inexperienced. Scientific founders should also be aware that they might have to switch positions to attract more desirable investors. Our results are important for VC investors as well. First, given the required expertise and network structure to guide young biotech firms, it might be a better strategy for inexperienced investors to act only as nonlead investors in syndicates with more experienced peers. Second, VC investors should be aware that even when they are experienced, they do not necessarily have access to the entire range of early stage investment opportunities. Active deal origination is critical to increase the supply of high-quality proposals where investors have the first option to invest.

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